UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,566	04/07/2005	Alan Barge	056291-5202	8993

9629 7590 02/26/2009

MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
CARTER, KENDRA D	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/26/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,566	BARGE, ALAN	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/7/05;10/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-12 are pending and examined on the merits.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 7-12 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 7-12 are rejected under 35 U.S.C. 101 based on the theory that the claims are directed to neither a method of making nor a method of using, but rather embraces or overlaps two different statutory classes of invention set forth in 35 U.S.C. 101, which is drafted so as to set forth the statutory classes of invention. 35 U.S.C.101 clearly states, "Whoever invents or discovers any new and useful process, machine,

manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title." The term process as defined by 35 U.S.C. 101 means "process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." This is not interpreted to mean that a patent can be issued on a process of preparation and a method of use. A patent is given to any new and useful process not processes. Thus, Claims 7-12 are rejected under 35 U.S.C. 101 for the reasons stated above.

Claim Rejections - 35 USC § 112

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-12 provide for the use of ZD6126 and gemcitabine, but since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Thus, claims 7-12 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(1) Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruns et al. (Clinical Cancer Research, May 2000, vol. 6, pp. 1936-1948) in view of Siemann et al. (Radiotherapy and oncology, 2000, vol. 57, pp. 5-12).

Bruns et al. teach epidermal growth factor receptor blockade with the angiogenesis compound C225 and gemcitabine result in significant antitumor effects in human pancreatic cancer (see title and page 1944, discussion, lines 1-7). Data indicate that therapy with C225 and C225 plus gemcitabine, but not gemcitabine alone, caused not merely an inhibition but an actual involution of the neovasculature (i.e. vascular damaging effects), leading to tumor cell apoptosis and regression of established tumors (see page 1944, discussion, column 1, last 6 lines). The mice were administered C225 on Tuesday and Friday and gemcitabine on Wednesday and Saturday for 32 days (see page 1938, column 1, lines 1-10).

Bruns et al. does not teach ZD6126 or an effective amount of ionizing radiation.

Siemann et al. teach that radiotherapy is the most important non-surgical treatment for cancer. Today, 45-50% of all cancer patients can be cured, and about 70% of those who are cured receive either radiation alone or in combination with other modalitites (see page 5, introduction, lines 1-5). Recent experimental data from several laboratories have demonstrated that vascular targeting strategies can effectively enhance the antitumor effects of radiation treatment. It is well established that the aberrant vascular morphology, spatial heterogeneity in vessels, and metabolic micro-environment associated with solid tumors, can have significant adverse effects on the efficacy of radiation therapy. Treatment with anti-vascular agents eliminates many of these problem areas by causing extensive hemorrhagic necrosis in the center of tumors. For example, agents such as CA4Dp and ZD6126 as well as the FAA analog, dimethylxanthenone acetic acid, can produce abrupt and significant vascular effects which ultimately lead to extensive ischemic tumor cell death. These agents may improve the radiation response of tumors by impacting the radiation refractory hypoxic cell subpopulation of tumors. Typically, the vascular shutdown and subsequent induction of necrosis after treatment with anti-vascular agents is not complete, thus leaving areas of viable tumor cells from which the tumor could regrow. These findings are consistent with the notion that the two treatments (radiation and vascular targeting agent) are acting in a complimentary fashion at the microregional level, ie. the vascular targeting agent is preferentially eliminating the poorly oxygenated, and hence, radio resistant tumor cell subpopulation (see page 8, column 1, first paragraph, last 5 lines to column 2, fist paragraph).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Bruns et al. and ZD6126 and radiation because of the following teachings: 1) Bruns et al. teach that an angiogenesis compound and gemcitabine cause actual involution of the neovasculature (i.e. vascular damaging effects) that leads to tumor cell apoptosis and regression of established tumors, compared to gemcitabine administered alone (see page 1944, discussion, column 1, last 6 lines); 2) Siemann et al. teach that ZD6126 is an angiogenesis compound that produce abrupt and significant vascular effects which ultimately lead to extensive ischemic tumor cell death (se page 8, column 1, paragraph 2, lines 5-10); 3) Selection of a known material based on its suitability for its intended use is obvious absent a clear showing of unexpected results attributable to the Applicant's specific selection. See e.g., *In re Leshin*, 227 F.2d 197, 125 USPQ 416 (CCPA 1960); and 4) Siemann et al. teach that typically the vascular shutdown and subsequent induction of necrosis after treatment with anti-vascular agents is not complete, thus leaving areas of viable tumor cells from which the tumor could re-grow (see page 8, column 1, last 8 lines); and 5) Siemann et al. further teach that because of the above, the notion that the two treatments (radiation and vascular targeting agent) are acting in a complimentary fashion at the microregional level, ie. the vascular targeting agent is preferentially eliminating the poorly oxygenated, and hence, radio resistant tumor cell subpopulation (see page 8, column 1, first paragraph, last 5 lines to column 2, fist paragraph). Thus, one skilled in the art would be motivated to substitute the angiogenesis compound or Bruns et al. with ZD6126 with expectation that the combination with

gemcitabine will be more effective in treating cancer. Further, one skilled in the art would be motivated to provide ionising radiation to the treatment because radiation therapy is seen as a complimentary therapy to anti-vascular agents in order to combate viable tumor cells not destroyed by the anti-vascular agent.

(2) Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruns et al. (Clinical Cancer Research, May 2000, vol. 6, pp. 1936-1948) in view of Siemann et al. (Radiotherapy and oncology, 2000, vol. 57, pp. 5-12) as applied to claims 1-4 above in further view of Nugiel et al. (US 6,291,504 B1).

The teachings of Bruns et al. and Siemann et al. are as applied to claims 1-4 above.

Bruns et al. and Siemann et al. do not teach a pharmaceutical composition comprising ZD6126 and gemcitabine in association with a pharmaceutically acceptable excipient or carrier (claim 5), or a kit comprising ZD6126 and gemcitabine (claim 6).

Nugiel et al. teach a combination therapy of an angiogenesis compound and one or more other known anti-cancer or anti-proliferative agents, such as gemcitabine (see abstract and column 11, lines 60-63, column 12, line 46). The combination therapy can be provided in a pharmaceutical kit (see column 13, lines 39-63; addresses claim 6). The formulation may be presented in unit-dose or multi-dose containers with sterile carriers (see column 35, lines 32-40 and column 36, lines 27-35).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Bruns et al. in view of Siemann et al. and a kit and pharmaceutical composition because the construction of compositions and kits are within the skill of the art for anti-cancer combination therapy as taught by Nugiel et al.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kendra D Carter/
Examiner, Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617